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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	24

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/282,239	GOLDMAN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,21,22 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,21,22,27 and 28* is/are rejected.

7)☒ Claim(s) *25,26 and 29* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants cancellation of claims 23-24, amendment of claims 25 and 26, and addition of new claims 27-29 is acknowledged. Applicants filing of a declaration under 1.132, Paper No. 23, 11/1/2002, is also acknowledged. Claims 19 and 21; 22, and 25-29 are at issue and are present for examination.

Applicants' arguments filed on 11/1/2002, paper No. 22, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 25, 26 and 29 are objected to because of the following informalities: Claims 25, 26 and 29 depend from rejected claim 19. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time

the application was filed, had possession of the claimed invention. The recitation in claims 27 and 29 to percent of purity of the claimed preparation of human mitotic oligodendrocyte progenitors, 90 % pure (claim 27) and 99% pure (claim 28) is not supported by the original specification and is therefore considered new matter. While applicants submit that support for such claims can be found in the data of Figures 5 A-B, this is not apparent, as Figures 5A-5B contain FACS data that does not appear to be quantifiable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19, 21 and 22 remain rejected under 35 U.S.C. 102(b) as being anticipated by Armstrong et al. (Journal of Neuroscience 12 (4): 1538-1547, April 1992).

This rejection is stated in a previous office action, Paper No. 9, 12/5/2000, traversed in Paper No. 12, 6/11/2001, and Paper No. 22, 11/1/2002 and maintained in Paper Nos. 13 and 21. The original rejection is repeated below for applicants convenience.

Armstrong et al. teach the existence and preparation of preparations enriched in human postnatal oligodendrocytes and oligodendrocyte progenitor cells. Specifically

Armstrong et al. characterize the glial cell population of adult human white matter after culturing in defined medium for 1-2 weeks (see Results pages 1540-1541 and Figure 2). Armstrong teach cultures which are enriched and substantially pure for both oligodendrocytes and pre-oligodendrocytes cells (See Figures 1-3 and supporting text on pages 1539-1542).

Claims 19, 21 and 22 are currently drawn to an enriched or purified preparation of human mitotic oligodendrocyte progenitor cells, wherein said cells are from a post-natal (Claim 21) or adult (Claim 22) human.

Applicants traverse that Armstrong et al. inherently produces the claimed enriched or purified preparation of human mitotic oligodendrocyte progenitor cells. The inherency of the claimed cell type in the taught preparation is based on the fact that both Armstrong and applicants used a similar initial procedure to obtain cells from a similar source.

Applicants traverse this on two basis. First applicants assert that Armstrong attempts the use of monoclonal O4-defined separation of the oligodendrocyte progenitor cells, a method previously shown effective in isolating oligodendrocyte progenitor cells from rats. Applicants submit that conversely applicants used the CNP/2 promoter-based separation. This argument is not found persuasive, because as stated previously, Armstrong et al., specifically teach a preparation comprising "fresh human temporal lobe obtained from biopsies of patients undergoing therapeutic resection for intractable epilepsey which had menginges, blood vessels and the majority of gray matter removed from before mincing" (See page 1539 under *Glial Cell Isolation*). On

page 16 of the instant specification, applicants teach that the claimed mitotically active human oligodendrocyte progenitor cells were isolated from adult human brain tissues obtained from lobectomy of epilepsey patients. Armstrong et al.'s preparation, which was similar to applicants initial preparations, constitutes an "enriched or purified preparation".

Applicants further traverse this rejection on the basis that the tissue extraction techniques used by Armstrong et al. were substantially and critically different from applicants. Applicants submit that Armstrong et al. describes an isolation procedure in which white matter was subjected to various enzymatic treatment solutions which comprised trypsin, and applicants choose not to use trypsin because they discovered that trypsin when used in applicants procedure to digest white matter was so destructive that it caused the loss of both oligodendrocytes and oligodendrocyte progenitor cells. Thus applicant conclude that there is no basis to assume that Armstrong et al. and applicants produce the same material. This argument is not found persuasive because while it is acknowledged that Armstrong and applicants have not produced the same material, the question is whether applicants claims read on the material produced by Armstrong et al. Applicants submit that in applicants hands, the use of trypsin is deleterious to oligodendrocytes and oligodendrocyte precursor cells, but there remains the question as to the concentrations of trypsin used and length of cell exposure to trypsin used by applicants compared with the procedure used by Armstrong et al. Thus as concentration and time of exposure to the trypsin are important factors in the dissociation of tissues, it remains to be seen whether the trypsin used by Armstrong et

al. would have destroyed both oligodendrocytes and oligodendrocyte precursor cells as suggested by applicants.

Further applicants attention is directed to Armstrong et al. (page 1543, right column and page 1540, right column, *Tissue Print*) where they describe the preparation of tissue prints of adult human white matter, in which pre-oligodendrocytes were consistently found. The enzyme solution used in these "tissue prints" comprised papain, collagenase and DNase I. The preparation of these tissue prints did not involve the use of the enzyme trypsin.

Thus claims 19, 21 and 22 remain anticipated by Armstrong et al.

Claims 19 and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Kirschenbaum et al. (Cerebral Cortex 6: 576-589, Nov/Dec 1994).

This rejection is stated in a previous office action, Paper No. 9, 12/5/2000, traversed in Paper No. 12, 6/11/2001, and Paper No. 22, 11/1/2002. The original rejection is repeated below for applicants convenience.

Kirschenbaum et al. teach that cells derived from the subependymal zone (SZ) and periventricular white matter of the adult human forebrain can indeed generate and differentiate into neurons in culture. Kirschenbaum et al. teach the culturing of adult human temporal lobe tissue samples in a defined medium for 7-28 days at which point the cell populations were characterized by immunocytochemistry, ^{3}H-thymidine labeling, calcium imaging and cellular morphology. Specifically Kirschenbaum et al. teach that subcortical white matter cultures are enriched in $O4^{+}$ oligodendrocytes and fiborous

astrocytes (See page 581, *Subcortical Phenotypes*), while the SZ comprises precursors that embarked upon neural differentiation (See page 584, *Source of the Neuronal Precursor Cells* and page 585, right column, second paragraph). Thus, Kirschenbaum et al. anticipate claims 19 and 21-22 to an enriched or purified preparation of human oligodendrocytes progenitor cells, , wherein said cells are from a post-natal or adult human.

Applicants continue to traverse this rejection on the basis that Kirschenbaum et al. does not disclose mitotic oligodendrocyte progenitor cells, thus the rejection should be withdrawn. Applicants position is further supported by the declaration of Dr. Goldman, Paper No. 20.

Applicants submit the recitation from page 582 of Kirschenbaum et al. from which applicants conclude that all of the oligodendrocytes were post-mitotic. In response to this specifically recited passage, applicants attention was directed to the recitation which directly follows the above passage which states"... In contrast, a second comparatively uncommon category of $O4^+$ cells was characterized by a larger (15-25 mm), flatter, and more substrate-apposed soma; each cell projected several relatively thick, long and tapering, unbranched processes. These cells constituted <1% of the $O4^+$ population, and frequently incorporated ^{3}H-thymidine. The onotogeny and fate of these $O4^+/^3$H-thymidine+ cells are now being evaluated separately..." This second passage clearly teaches that the preparation of Kirschenbaum et al. did comprise a substantially pure mitotically active O4+ cell population, albeit a small population.

Applicants traverse this argument on the basis that this second category of $O4^+$ cells do not include human mitotic oligodendrocyte progenitor cells as claimed (Second Goldman Declaration paragraph 8). Applicants submit that the claimed human mitotic oligodendrocyte progenitor cells are initially $O4^-$, are small bodies with diameters of less than 10 um and have an ovoid morphology, in contrast to the second category of cells characterized by Kirschenbaum et al. Thus applicants conclude that the Kirschenbaum et al.'s second category of cells do not constitute human mitotic oligodendrocyte progenitor cells as claimed. This argument is not found persuasive, based on applicants statements that "... this second category of $O4^+$ cells do not include human mitotic oligodendrocyte progenitor cells as claimed". While it is understood that the cell population identified by applicants (i.e. mitotically active, $O4^-$ and displaying the characteristics discussed above) are distinct from Kirschenbaum et al.'s second category of cells, it is not clear that Kirschenbaum et al.'s second category of cells did not include human mitotic oligodendrocyte progenitor cells as originally stated. Applicants statements in paragraph 8 of the accompanying declaration that "this second category of O4+ cells does not include human mitotic oligodendrocyte progenitor cells is not supported by any evidence. Applicants merely provide evidence as to how Kirschenbaum et al.'s second category of cells is different from applicants population of cells. Further, applicants statements that "Human mitotic oligodendrocyte progenitor cells are initially O4-..." is not consistent with applicants earlier statements in the same declaration (paragraph 5) that "the use of monoclonal antibody O4-defined separation of

the oligodendrocyte progenitor cells" is a method previously shown effective in isolating oligodendrocyte progenitor cells from rats.

Irregardless of whether or not Kirschenbaum et al. teach the presence of mitotically active human oligodendrocytes progenitor cells in the taught preparations, as discussed above, with respect to the preparation of Armstrong et al., Kirschenbaum et al. teach a preparation comprising "adult human temporal lobe obtained during anterior temporal lobectomy of epilepsey patients followed by dissociation for single-cell monolayer culture (See page 577 under *Tissue Samples* and *Culture preparation*) which constitutes an "enriched or purified preparation". While it is acknowledged that Kirschenbaum et al. did not identify pre-oligodendrocytes nor oligodendrocytes which incorporated ^{3}H-thymidine *in vitro* in response to certain specific stimuli, the preparation taught by Kirschenbaum et al. does comprise human mitotic oligodendrocyte progenitor cells and their presence is an inherent property of the "enriched or purified preparation" taught by Kirschenbaum et al. The basis of the presence of the mitotically active human oligodendrocyte progenitor cells in the preparation of Kirschenbaum et al. is that this preparation is similar to that preparation used by applicants to further isolate the claimed mitotically active human oligodendrocyte progenitor cells. Specifically, on page 16 of the instant specification, applicants teach that the claimed mitotically active human oligodendrocyte progenitor cells were isolated from adult human brain tissues obtained from lobectomy of epilepsey patients.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
January 24, 2003